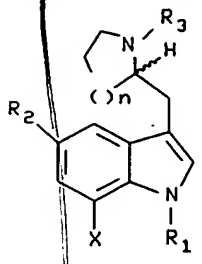
CLAIMS

1. A compound of the formula



I

wherein n is 0, 1, or 2; X is hydrogen, chlorine, bromine, or iodine; R_1 is hydrogen; R_2 is selected from hydrogen, halogen, cyano, $-OR_4$, $-(CH_2)_m-(C=O)NR_5R_6$, $-(CH_2)_m-SO_2NR_5R_6$, $-(CH_2)_m-NR_7(C=O)R_8$, $-(CH_2)_m-NR_7SO_2R_8$, $-(CH_2)_m-S(O)_xR_8$, $-(CH_2)_m-NR_7(C=O)NR_5R_6$, $-(CH_2)_m-NR_7(C=O)OR_9$, and $-CH=CH(CH_2)_yR_{10}$; R_3 is selected from hydrogen and C_1 to C_6 linear or branched alkyl; R_4 is selected from hydrogen, C_1 to C_6 alkyl, and aryl; R_5 and R_6 are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl or R_5 and R_6 taken together to form a 4, 5, or 6 membered ring; R_7 and R_8 are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl; R_9 is selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl; R_{10} is selected from $-(C=O)NR_5R_6$ and $-SO_2NR_5R_6$, wherein R_5 and R_6 are defined as above, and $-NR_7(C=O)R_8$, $-NR_7SO_2R_8$, $-NR_7(C=O)NR_5R_6$, $-S(O)_xR_8$ and $-NR_7(C=O)OR_9$, wherein R_7, R_8, and R_9 are as defined above; y is 0, 1, or 2; x is 1 or 2; m is 0, 1, 2, or 3; and the above aryl groups and the aryl moieties of the above alkylaryl groups are independently selected from phenyl and substituted phenyl, wherein said substituted phenyl may be substituted with one to three groups selected from C_1 to C_4 alkyl, halogen, hydroxy, cyano, carboxamido, nitro, and C_1 to C_4 alkoxy, with the proviso that when R_2 is hydrogen or $-OR_4$ and R_4 is hydrogen, n is 0 or 1, and the pharmaceutically acceptable salts thereof.

2. The R enantiomer of a compound according to claim 1.

3. A compound according to claim 1 wherein R_1 is hydrogen; R_2 is ~~$-(CH_2)_m-SO_2NHR_5$~~, $-(CH_2)_m-NHSO_2R_8$, $-(CH_2)_m-SO_2R_8$, $-(CH_2)_m-(C=O)NHR_5$, or $-(CH_2)_m-NH(C=O)R_8$; R_3 is hydrogen or methyl; and m, R_5 and R_8 are as defined in claim 1.

4. A compound according to claim 1, said compound being selected from:

(R)-5-methoxy-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-bromo-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-ethylsulfonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-methylaminosulfonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-carboxamido-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-methylsulfonylethyl)-3-(N-methylpyrrolidin-2-yl-methyl)-1H-indole;

(R)-5-(2-methylsulfonamidoethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-aminosulphonylethenyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-aminosulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-N,N-dimethylaminosulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-phenylsulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole hemisuccinate;

(R)-5-(2-ethylsulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole hemisuccinate;

(R)-5-(2-phenylsulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(3-benzenecarbonylaminoprop-1-enyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-(4-methylphenylsulphonyl)ethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(3-methylsulphonylaminoprop-1-enyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-ethylsulphonylethyl)-3-(N-2-propylpyrrolidin-2-ylmethyl)-1H-indole;

(R)-5-(2-ethylsulphonylethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole; and

(R)-7-Bromo-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole.

5. A pharmaceutical composition for treating a condition selected from hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, and chronic paroxysmal hemicrania and headache associated with vascular disorders comprising an amount of a compound according to claim 1 effective in treating such condition and a pharmaceutically acceptable carrier.

6. A pharmaceutical composition for treating disorders arising from deficient serotonergic neurotransmission comprising an amount of a compound according to claim 1 effective in treating such a disorder and a pharmaceutically acceptable carrier.

7. A method for treating a condition selected from hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache associated with vascular disorders comprising administering to a mammal requiring such treatment an amount of a compound

according to claim 1 effective in treating such condition.

8. A method for treating disorders arising from deficient serotonergic neurotransmission comprising administering to a mammal requiring such treatment an amount of a compound according to claim 1 effective in treating such a disorder.

9. The compound 5-(2-phenylsulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole or a pharmaceutically acceptable salt thereof.

10. A compound according to claim 9, wherein the compound is (R)-5-(2-phenylsulphonylethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole.

11. The compound 5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole or a pharmaceutically acceptable salt thereof.

12. A compound according to claim 11, wherein the compound is (R)-5-(methylaminosulfonylmethyl)-3-(N-methylpyrrolidin-2-ylmethyl)-1H-indole.

13. A pharmaceutical composition for treating a condition selected from hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, and chronic paroxysmal hemicrania and headache associated with vascular disorders comprising an amount of a compound according to claim 12 ranging from 0.1μg to 200mg effective in treating such condition and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition for treating disorders arising from deficient serotonergic neurotransmission comprising an amount of a compound according to claim 12 ranging from 0.1μg to 200mg effective in treating such a disorder and a pharmaceutically acceptable carrier.

15. A method for treating a condition selected from hypertension, depression, anxiety, eating disorders,

obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache associated with vascular disorders comprising administering to a mammal requiring such treatment an amount of a compound according to claim 12 ranging from 0.1μg to 200mg effective in treating such condition.

16. A method for treating disorders arising from deficient serotonergic neurotransmission comprising administering to a mammal requiring such treatment an amount of a compound according to claim 12 ranging from 0.1μg to 200mg effective in treating such a disorder.

17. The compound 5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole or a pharmaceutically acceptable salt thereof.

18. A compound according to claim 17, wherein the compound is (R)-5-(methylaminosulfonylmethyl)-3-(pyrrolidin-2-ylmethyl)-1H-indole.

19. A pharmaceutical composition for treating a condition selected from hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, and chronic paroxysmal hemicrania and headache associated with vascular disorders comprising an amount of a compound according to claim 18 ranging from 0.01μg to 200mg effective in treating such condition and a pharmaceutically acceptable carrier.

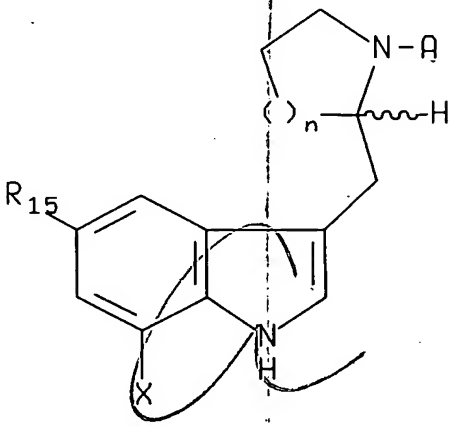
20. A pharmaceutical composition for treating disorders arising from deficient serotonergic neurotransmission comprising an amount of a compound according to claim 18 ranging from 0.01μg to 200mg effective in treating such a disorder and a pharmaceutically acceptable carrier.

21. A method for treating a condition selected from hypertension, depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain and chronic paroxysmal hemicrania and headache associated

with vascular disorders comprising administering to a mammal requiring such treatment an amount of a compound according to claim 18 ranging from 0.01μg to 200mg effective in treating such condition.

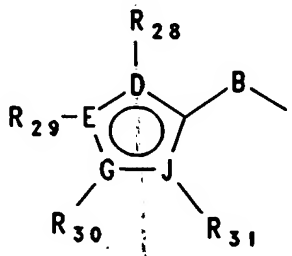
22. A method for treating disorders arising from deficient serotonergic neurotransmission comprising administering to a mammal requiring such treatment an amount of a compound according to claim 18 ranging from 0.01μg to 200mg effective in treating such a disorder.

23. A process for preparing a compound of the formula



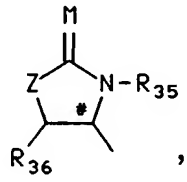
(XVI)

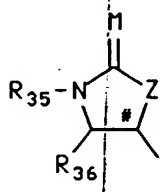
wherein X is chlorine, bromine, or iodine; R_{11} is a first suitable nitrogen protecting group; R_{15} is hydrogen, halogen, cyano, $-OR_{16}$, $-(CH_2)_m-(C=O)NR_{17}R_{18}$, $-(CH_2)_m-SO_2NR_{17}R_{18}$, $-(CH_2)_m-NR_{19}(C=O)R_{20}$, $-(CH_2)_m-NR_{19}SO_2R_{20}$, $-(CH_2)_m-S(O)_xR_{20}$, $-(CH_2)_m-NR_{19}(C=O)NR_{17}R_{18}$, $-(CH_2)_m-NR_{19}(C=O)OR_{21}$, $-CH=CH(CH_2)_yR_{22}$, $-(CH_2)_m-T$, and a substituent of the formula

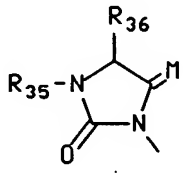


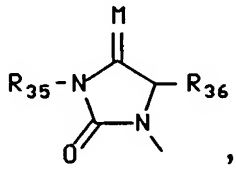
;

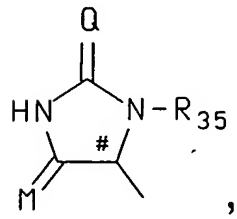
B represents a direct bond, C_1-C_4 alkyl, or C_1-C_4 alkenyl; D, E, G, and J are each independently oxygen, sulfur, nitrogen or carbon, provided that at least one of D, E, G, and J is nitrogen; R_{28}, R_{29}, R_{30}, and R_{31} are each independently hydrogen, C_1-C_6 alkyl, aryl, C_1-C_3 alkylaryl, C_1-C_3 alkylheteroaryl, halogen, cyano, trifluoromethyl, nitro, $-OR_{32}$, $-NR_{32}R_{33}$, $-(CH_2)_mOR_{32}$, $-SR_{32}$, $-SO_2NR_{32}R_{33}$, $-NR_{32}SO_2R_{33}$, $-NR_{32}CO_2R_{33}$, $-CONR_{32}R_{33}$, or $-CO_2R_{32}$; one of R_{28} and R_{29}, R_{29} and R_{30}, or R_{30} and R_{31} may be taken together to form a five- to seven-membered alkyl ring, a six-membered aryl ring, a five- to seven-membered heteroalkyl ring having 1 heteroatom of N, O, or S, or a five- to six-membered heteroaryl ring having 1 or 2 heteroatoms of N, O, or S; R_{32} and R_{33} are each independently hydrogen, C_1 to C_6 alkyl, $-(CH_2)_qR_{34}$, C_1 to C_3 alkylaryl, or aryl; R_{32} and R_{33} may be taken together to form a C_4-C_7 alkyl ring; R_{34} is cyano, trifluoromethyl, or C_1-C_4 alkoxy; R_{16} is selected from hydrogen, C_1 to C_6 alkyl, and aryl; T is

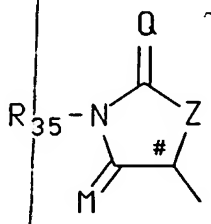

(i)


(ii)

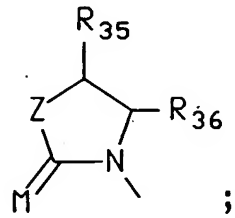

(iii)


(iv)


(v)


(vi)

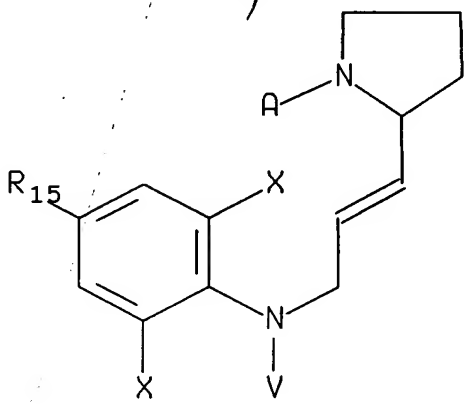
or


(vii)

M and Q are each independently oxygen or sulfur; Z is -O-, -S-, -NH, or $-CH_2$; R_{35} and R_{36} are each independently

hydrogen, C_1 to C_6 alkyl, aryl, C_1 to C_3 alkylaryl, or C_1 to C_3 alkylheteroaryl; R_{22} is selected from $-(C=O)NR_{23}R_{24}$, $-SO_2NR_{23}R_{24}$, $-NR_{25}(C=O)R_{26}$, $-NR_{25}SO_2R_{26}$, $-NR_{25}(C=O)NR_{23}R_{24}$, $-S(O)_xR_{26}$ and $-NR_7(C=O)OR_{27}$; R_{17}, R_{18}, R_{23}, and R_{24} are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl, or R_{17} and R_{18} or R_{23} and R_{24} maybe taken together to form a 4, 5, or 6 membered ring; R_{19}, R_{20}, R_{21}, R_{25}, R_{26}, and R_{27} are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl; y is 0, 1, or 2; x is 1 or 2; m is 0, 1, 2, or 3; n is 0, 1 or 2; q is 1, 2, or 3; a first chiral carbon designated by *; a second chiral carbon designated by #; and the above aryl groups and the aryl moieties of the above alkylaryl groups are independently selected from phenyl and substituted phenyl, wherein said substituted phenyl may be substituted with one to three groups selected from C_1 to C_4 alkyl, halogen, hydroxy, cyano, carboxamido, nitro, and C_1 to C_4 alkoxy,

comprising, performing a transition metal catalyzed cyclization on a compound of the formula



(XVII)

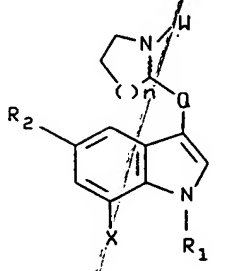
wherein R_{11} and R_{15} are as defined above and V is a second suitable nitrogen protecting group.

24. The process of claim 23, wherein X is bromine.

25. The process of claim 23, wherein A is benzyloxycarbonyl.

26. The process of claim 23, wherein V is trifluoroacetyl.

27. A compound of the formula



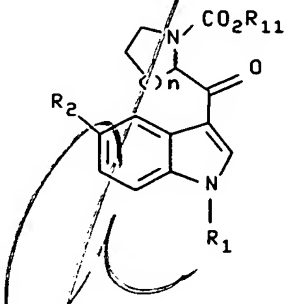
V

wherein X is hydrogen, bromine, chlorine, or iodine; W is $-CO_2R_{11}$ or R_3; Q is CH_2 or C=O; n is 0, 1 or 2; R_1 is hydrogen; R_2 is selected from halogen, cyano, $-OR_4$, $-(CH_2)_m-(C=O)NR_5R_6$, $-(CH_2)_m-SO_2NR_5R_6$, $-(CH_2)_m-NR_7(C=O)R_8$, $-(CH_2)_m-NR_7SO_2R_8$, $-(CH_2)_m-S(O)_xR_8$, $-(CH_2)_m-NR_7(C=O)NR_5R_6$, $-(CH_2)_m-NR_7(C=O)OR_9$, and $-CH=CH(CH_2)_yR_{10}$; x is 1 or 2; m is 0, 1, 2, or 3; R_3 is selected from hydrogen and C_1 to C_6 linear or branched alkyl; R_4 is selected from hydrogen, C_1 to C_6 alkyl, and aryl, R_5 and R_6 are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl or R_5 and R_6 taken together to form a 4, 5, or 6 membered ring; R_7 and R_8 are independently selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl; R_9 is selected from hydrogen, C_1 to C_6 alkyl, aryl, and C_1 to C_3 alkyl-aryl; R_{10} is selected from $-(C=O)NR_5R_6$ and $-SO_2NR_5R_6$, wherein R_5 and R_6 are defined as above, and $-NR_7(C=O)R_8$, $-NR_7SO_2R_8$, $-NR_7(C=O)NR_5R_6$, $-S(O)_xR_8$ and $-NR_7(C=O)OR_9$, wherein R_7, R_8, R_9 and x are defined as above; y is 0, 1, or 2; R_{11} is selected from C_1 to C_6 alkyl, benzyl and aryl; and the above aryl groups and the aryl moieties of the above alkyl-aryl groups are independently selected from phenyl and substituted phenyl, wherein said substituted phenyl may be substituted with one to three groups selected from C_1 to C_4 alkyl, halogen, hydroxy, cyano, carboxamido, nitro,

and C_1 to C_4 alkoxy, with the proviso that when W is R_3, Q is C=O, and with the proviso that when X is bromine, chlorine, or iodine, W is $-CO_2R_{11}$ and Q is CH_2.

28. The R enantiomer of a compound according to claim 27.

29. A compound according to claim 27, said compound being a compound of the formula



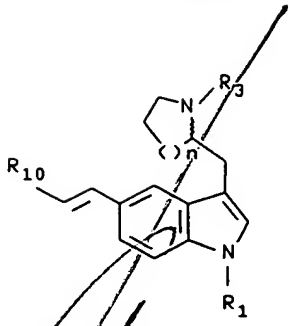
II

wherein n, R_1, R_2 and R_{11} are as defined in claim 29.

30. The R enantiomer of a compound according to claim 29.

31. A compound according to claim 29 wherein R_1 is hydrogen; R_2 is $-(CH_2)_m-SO_2NHR_5$, $-(CH_2)_m-NHSO_2R_8$, $-(CH_2)_m-SO_2R_8$, $-(CH_2)_m-(C=O)NHR_5$ or $-(CH_2)_m-NH(C=O)R_8$; m is 0, 1, 2, or 3; R_5 is hydrogen, C_1 to C_6 alkyl, aryl, or C_1 to C_3 alkyl-aryl; R_{11} is selected from C_1 to C_6 alkyl, benzyl and aryl; and the above aryl groups and the aryl moieties of the above alkylaryl groups are independently selected from phenyl and substituted phenyl, wherein said substituted phenyl may be substituted with one to three groups selected from C_1 to C_4 alkyl, halogen, hydroxy, cyano, carboxamido, nitro, and C_1 to C_4 alkoxy.

32. A compound according to claim 27, said compound being a compound of the formula



III

wherein n, R_1, R_3 and R_{10} are as defined in claim 27.

33 ~~32~~. The R enantiomer of a compound according to claim 31.

34 ~~33~~. A compound according to claim 31 wherein R_1 is hydrogen; R_3 is hydrogen or methyl; and R_{10} is $-SO_2NHR_5$, $NHSO_2R_8$, $-SO_2R_8$, $-(C=O)NHR_5$ or $-NH(C=O)R_8$, wherein R_5 and R_8 ~~are as defined in claim 27.~~